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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,882	08/17/2005	Michael Lyne	GJE-7477	1606
23557 7590 07/09/2007 SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION PO BOX 142950 GAINESVILLE, FL 32614-2950				
			EXAMINER KIM, JENNIFER M	
			ART UNIT 1617	PAPER NUMBER
			MAIL DATE 07/09/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/517,882	LYNE, MICHAEL	
	<b>Examiner</b>	<b>Art Unit</b>	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 2-9 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 21, 2007 has been entered.

#### ***Action Summary***

The rejection of claims 2-9 under 35 U.S.C. 112, first paragraph is hereby expressly withdrawn in view of Example in instant specification page 3 and Applicant's response.

The rejection of claim 9 under 35 U.S.C. 112, second paragraph is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 2-9 under 35 U.S.C. 103(a) as being unpatentable over Fasmer et al. (1987) of record in view of Williams et al. (WO02/00195 A2) of record is being maintained for the reasons stated in the previous Office Action.

#### ***Response to Arguments***

Applicant's arguments filed May 21, 2007 have been fully considered but they are not persuasive. Applicant argues that there is no motivation to combine Fasmer et al. with Williams et al. to arrive at the current invention because Williams et al. reference discloses nefopam (the racemate) as one of a long list of analgesics over 100 analgesics. This is not persuasive because Williams et al. teach that analgesic compositions that are useful for long-lasting pain relief from mucosal damage of the nasal cavity are preferred to be administered directly to the nasal cavity including the composition of nefopam in general. Therefore, one would have been motivated to employ (+)-nefopam taught by Fasmer et al. that is more potent form of nefopam in order to achieve long-lasting pain relief from mucosal damage in nasal cavity by intranasal administration as taught by Williams et al. Further, Williams et al.'s long list of analgesics of intranasal administration teach that intranasal administration is routine and commonly applied to many of analgesic agents for the treatment of pain including nefopam compounds. Applicant argues that William et al. described administration to mucosal surfaces other than nasal mucous membrane. This is not persuasive because instant claims are drawn to a composition claims not a "method of achieving systemic administration" and there is no structural difference between the claimed invention and the obvious composition of Fasmer et al. in view of Williams et al. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fasmer et al. (1987) of record in view of Williams et al. (WO02/00195 A2) of record.

Fasmer et al. teach the antinociceptive effects of (+)-nefopam in mice. (abstract). Fasmer et al. teach that the antinociceptive activity of (+)-nefopam was significantly more potent than (-)-nefopam. (abstract). **Fasmer et al. teach that (+)-nefopam was dissolved in 0.9% NaCl.** (page 508, under materials and methods). Fasmer's teaching of 0.9% **NaCl** to dissolve (+)-nefopam anticipates the claimed limitation of the "solubility enhancer" set forth in claim 3 because NaCl combined with (+)-nefopam promotes the dissolution of (+)-nefopam.

Fasmer et al. teach the antinociceptive effects of (+)-nefopam in mice. (abstract). Fasmer et al. teach that the antinociceptive activity of (+)-nefopam was significantly more potent than (-)-nefopam. (abstract). Fasmer et al. teach that (+)-nefopam was dissolved in 0.9% NaCl. (page 508, under materials and methods). Fasmer et al. teach that nefopam is an effective analgesic in man and its **analgesic activity** can also be demonstrated in some of **tests of nociception** in animals. (page 508, left-hand

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column). Fasmer et al. teach in conclusion, that (+)-nefopam is more potent as an **analgesic** than the (-) enantiomer. (page 511, right-hand, column, 3<sup>rd</sup> full paragraph).

Fasmer et al. do not teach the intranasal administration for treatment of pain set forth in claims 4, pain associated with cancer set forth in claim 8, the amount of (+) nefopam set forth in claim 9, the other agents set forth in claim 6, and the pH ranges set forth in claims 2, 4 and 7.

Williams et al. teach that the composition comprising **nefopam** is suitable for application to the mucous membrane of the nasal cavity to relieve pain. (page 12, line 16, abstract). Williams et al. teach that the **painful condition** and symptoms are endured by almost all **chemotherapy** patients. (page 1, lines 23-25). Williams et al. teach that the composition is preferably applied to a mucosal surface of the subject's nasal cavity. (page 3, lines 10-13). Williams et al. teach that the **pH** of the composition is within the range of from about **2 to about 9**, more preferably, about **3 to 7**, even more preferably **about 4 to about 5**, and optimally about **4.5**. (page 10, lines 26-28). These ranges encompasses and/or overlap and/or within Applicant's pH set forth in claims 2, 4 and 7. Williams et al. teach that **NMDA receptor antagonists**, a **non-steroidal anti-inflammatory agents**, **local anesthetics**, and **narcotic analgesics (opioids)** can be included in the composition and also suitable for application to nasal mucous cavity. (page 4, page 11, examples). Williams et al. teach that **mucoadhesives** can be also employed in the composition (page 7, lines 8-15).

It would have been obvious to one of ordinary skill in the art to modify the (+) nefopam formulation taught by Fasmer et al. to intranasal administration for treatment of

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pain because Williams et al. teach that nefopam comprising formulation in general are preferably applied directly to nasal cavity. One would have been motivated to make such a modification in order to employ preferred route of administration of nefopam known in the art as taught by Williams et al. It would have been obvious to one of ordinary skill in the art to adjust the pH of (+) nefopam formulation within about 3 to 7, even more preferably about 4 to 5 because Williams et al. teach the pH of nefopam suitable for intranasal application. One would have been motivated to optimize the pH of (+) nefopam suitable for intranasal application taught by Williams et al. in order to avoid any irritation in nasal cavity. It would have been obvious to one of ordinary skill in the art to further include other agents such as NMDA antagonist, non-steroidal anti-inflammatory agents set forth in claim 6, because these agents are also effective for the treatment of pain and suitable for the nasal mucosal application as taught by Williams et al. One of ordinary skill in the art would have been motivated to combine the agents set forth in claim 6, in order to achieve at least an additive effect in treatment of pain. It would have been obvious to one of ordinary skill in the art that Fasmer et al's (+) nefopam formulation as modified by Williams et al. is effective to treat pain including pain associated with cancer because Fasmer et al. teach that (+) nefopam is more potent as an analgesic than its enantiomer and because almost all cancer patients endure pain. There is a reasonable expectation of successfully treating pain associated with cancer with (+) nefopam nasal composition because (+) nefopam possess not only effective analgesic property but significantly more potent than its enantiomer, (-) nefopam, in man. Further, the nasal applicability of nefopam in general is well taught by

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Williams et al. with its suitable pH. The amount of (+) nefopam to be employed set forth in claim 9 is obvious because Fasmer teaches that nefopam is an effective analgesic agent in man. One would have been motivated to optimize the effective analgesic amounts in man as taught by Fasmer et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.


None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic

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Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Jennifer Kim  
Patent Examiner  
Art Unit 1617

Jmk  
July 3, 2007